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Evolution and the Need for Ascorbic Acid

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Abstract. Ascorbic acid differs from other vitamins in that an exogenous source is required by only a few animal species. It is pointed out that this fact indicates that the amount contained in a diet of raw natural plant food is less than the optimum intake, corresponding to the best health. This argument leads to the conclusion that the optimum daily intake is about 2.3 g or more, for an adult with energy requirement 2500 kcal day^{-1}.

Ascorbic acid(vitamin C) is required in his diet by man for life and good health. People who receive no ascorbic acid become sick with scurvy in a few weeks, and die in a few months.

Since the discovery of ascorbic acid and its identification with vitamin C there has been continued effort to determine the human requirement for this essential nutrient. Evidence indicates that the minimum daily intake needed to prevent scurvy is about 10 mg. The daily allowance recommended by health authorities for adults ranges from 20 mg in the United Kingdom to 75 mg in West Germany. The Food and Nutrition Board of the U.S. National Research Council[1] recommends values ranging from 35 mg for an infant to 60 mg for a 70-kg man, as designed for the maintenance of good nutrition of practically all healthy people in the U.S.A. The recommended allowances are said to provide a generous increment for individual variability and a surplus to compensate for potential losses in food.

These recommended values of the daily allowance of ascorbic acid have clearly resulted from a concentration by the authorities on the need to prevent scurvy. We may, however, ask whether larger amounts might not be needed to provide the optimum state of health. Numerous clinical reports indicate that large amounts of ascorbic acid are beneficial in increasing resistance to infections, improving the healing of wounds and burns, and decreasing the incidence of shock following injury or surgery. Moreover, ascorbic acid is nontoxic; it has been described[2] as probably the least toxic of all known substances of comparable physiologic activity. People have ingested 100 g per day for several days and 40 g per day for weeks without being harmed.

In a discussion of vitamin C and immunity to infection Bourne[3] in 1949 pointed out that the green foodstuffs eaten by the gorilla provide about 4.5 g of ascorbic acid per day, and that before the development of agriculture man existed largely on greens, supplemented with some meat. He concluded that "It may be possible, therefore, that when we are arguing whether 7 or 30 mg of vitamin C a day is an adequate intake we may be very wide of the mark. Perhaps we should be arguing whether 1 or 2 g a day is the correct amount." Stone[2,4,5] has suggested that the optimum rate of intake of ascorbic acid is about 3 g per day under ordinary conditions, and larger, up to 40 g per day, for a person under stress (for example, when infected with the virus of the common cold). Régnier[6] also recommends a large intake, 5 g per day or more, for averting or ameliorating the common cold. One of the arguments used by Stone is the following: the rat under normal conditions synthesizes ascorbic acid at the reported rate 26 mg day^{-1} kg^{-1} (see ref. 7) to 58 mg day^{-1} kg^{-1} (see ref. 8). If we assume proportionality to body weight (as indicated by the amount needed to prevent scurvy in the guinea pig), these correspond to 1.8–4.1 g day^{-1} for a 70-kg man.

Ascorbic acid differs from the other vitamins in that it is required in the diet by only a few species of animals—man, other primates, the guinea pig, an Indian fruit-eating bat, and the red-vented bulbul and some related species of Passeriform birds.[4,9] Other species of animals synthesize ascorbic acid. All mammals and other larger animals require vitamin A, thiamine, riboflavin, nicotinic acid, and pyridoxine as essential nutrients, although microorganisms usually have the power to synthesize all or most of these substances.

In the following paragraphs I point out that the fact that ascorbic acid is synthesized by most animal species, but not by man, provides strong evidence that the optimum rate of intake by man is about 2 or 3 g per day or more, 50–100 times, or more, the amounts recommended by the health authorities.

Let us consider the way in which man and other organisms have evolved. Initially there was on earth the "hot thin soup," containing molecules of millions, perhaps hundreds of millions of different kinds. Some molecules with autocatalytic ability appeared; they increased the rate of production of duplicates of themselves, probably by working as complementary pairs.[10] Some of them developed specific heterocatalytic ability, speeding up the production of certain molecules of other kinds. The development of a cell membrane favored the process, by keeping the cooperating molecules, especially nucleic acids and proteins, together.

There then followed the long eobiontic period, two or three billion years, during which there took place the astounding process of biochemical evolution, a much greater accomplishment than the process of morphological development and differentiation of larger organisms that occurred later. In this eobiontic period there were developed the genes to direct the synthesis of the enzymes required to catalyze great numbers of chemical reactions within the cell. The way in which this took place was discovered by Horowitz.[11] It may be illustrated by a discussion of thiamine. Molecules of thiamine were present in the original hot thin soup, and soon became essential to the functioning of the earliest unicellular forms of life. When the supply of thiamine had been nearly used up, and the organisms were competing for it, one organism underwent a mutation that permitted it to synthesize an enzyme that catalyzed the synthesis of thiamine from two other substances (pyrimidine pyrophosphate and thiazole phosphate) in the soup. This organism survived, while the others died from thiamine starvation (microbiological beriberi). Then, as the supply of pyrimidine pyrophosphate was being used up, an organism developed the gene to produce an enzyme to catalyze its synthesis from hydroxymethylpyrimidine and ATP (adenosine triphosphate), still present in the soup. Similarly, a gene was developed to produce an enzyme to make thiazole phosphate from thiazole and ATP. Several other steps were developed, until the organism was able to synthesize thiamine from substances present in large amounts in the environment. Many existing species of bacteria, fungi, and algae are able to synthesize thiamine, other vitamins, and all other essential organic substances.

When large, multicellular organisms developed, with specialized organs, some of these abilities became a handicap, and were lost. Let us continue with thiamine as an example. All mammals require thiamine in their food, in order to live. The ability to synthesize thiamine was lost by an early ancestral vertebrate, several hundred million or a billion years ago. This animal was ingesting plants, which provided an ample supply of thiamine, about 5 mg for each 2500 kcal of food energy. The synthetic mechanism was not needed, and it was a burden: it cluttered up the cells, added to the body weight, used energy that could be better used for other purposes. When a series of mutations occurred that eliminated this mechanism, the mutant was favored over the wild type, which failed to meet the competition and died out.[12] The victory of a mutant strain of a bacterium over the wild type in the competition for survival in the presence of an ample supply of the essential nutrient has been verified by direct experiments in the laboratory by Zamenhof and Eichhorn.[13]

In addition to thiamine, all mammalian species, so far as studied, require riboflavin, nicotinic acid, and vitamin A in their food. We conclude that the supply of food available to an earlier ancestor provided an adequate supply of these vitamins, enough to make it advantageous to discard the mechanism for synthesizing them. There is little doubt that this food was plant food, probably not greatly different from present day plant food.

In the recently published handbook on metabolism of the Federation of American Biological Handbooks[14] there is a table giving the amounts of four water-soluble vitamins (and also of vitamin A) in 366 raw and processed plant foods. I have recalculated the values to the basis of the quantity with energy value 2500 kcal (the average daily need of a man or woman) for the 110 raw natural plant foods listed in the table, with the results shown in Table 1.

I have pointed out[12] that an animal that synthesizes an essential substance synthesizes a somewhat smaller daily amount than the optimum, because to synthesize the optimum amount would require supporting the burden of additional synthetic machinery, with only a smaller compensation. Also, a mutant that has an exogenous source of the essential substance that provides somewhat less than the optimum amount may win the competition, because the wild type has to support the burden of machinery.

TABLE 1. *Water-soluble vitamin content (mg) of 110 raw natural plant foods (referred to amount giving 2500 kcal of food energy).*

	Thiamine	Riboflavin	Nicotinic acid	Ascorbic acid
Nuts and grains (11)	3.2	1.5	27	0
Fruit, low-C (21)	1.9	2.0	19	600
Beans and peas (15)	7.5	4.7	34	1000
Berries, low-C (8)	1.7	2.0	15	1200
Vegetables, low-C (25)	5.0	5.9	39	1200
Intermediate-C foods (16)	7.8	9.8	77	3400
Collards	10.8	17	92	5000
Chives	7.1	11.6	45	5000
Cabbage	6.2	5.0	32	5100
Brussels sprouts	5.6	8.9	50	5700
Cauliflower	10.0	9.3	65	7200
Mustard greens	8.9	18	65	7800
Kale	...	...	...	8200
Broccoli spears	7.8	18	70	8800
Black currants	2.3	2.3	14	9300
Parsley	6.8	15	68	9800
Hot red chili peppers	3.8	7.7	112	14200
Sweet green peppers	9.1	9.1	57	14600
Hot green chili peppers	6.1	4.1	115	15900
Sweet red peppers	6.5	6.5	40	16500
Average for 110 foods	5.0	5.4	41	2300

Nuts and grains: almonds, filberts, macadamia nuts, peanuts, barley, brown rice, whole grain rice, sesame seeds, sunflower seeds, wild rice, wheat.

Fruit (low in vitamin C, less than 2500 mg): apples, apricots, avocadoes, bananas, cherries (sour red, sweet), coconut, dates, figs, grapefruit, grapes, kumquats, mangoes, nectarines, peaches, pears, pineapple, plums, crabapples, honeydew melon, watermelon.

Beans and peas: broad beans (immature seeds, mature seeds), cowpeas (immature seeds, mature seeds), lima beans (immature seeds, mature seeds), mung beans (seeds, sprouts), peas (edible pod, green mature seeds), snapbeans (green, yellow), soybeans (immature seeds, mature seeds, sprouts).

Berries (low-C, less than 2500 mg): blackberries, blueberries, cranberries, loganberries, raspberries, currants, gooseberries, tangerines.

Vegetables (low-C, less than 2500 mg): bamboo shoots, beets, carrots, celeriac root, celery, corn, cucumber, dandelion greens, eggplant, garlic cloves, horseradish, lettuce, okra, onions (young, mature), parsnips, potatoes, pumpkins, rhubarb, rutabagas, squash (summer, winter), sweet potatoes, green tomatoes, yams.

Intermediate-C foods (2500–4900 mg): artichokes, asparagus, beet greens, cantaloupe, chicory greens, chinese cabbage, fennel, lemons, limes, oranges, radishes, spinach, zucchini, strawberries, swiss chard, ripe tomatoes.

In Table 2 there are given the average amounts (per 2500 kcal of food energy) of thiamine, riboflavin, nicotinic acid, and ascorbic acid for the 110 natural foods listed in Table 1, the recommended daily allowances of the four vitamins, and the ratios of the two quantities.

It is interesting that for thiamine, riboflavin, and nicotinic acid the values of the ratio of the amount in the foods to the recommended daily allowance (both

TABLE 2. *Comparison of average vitamin content (mg) of 110 raw natural plant foods with the recommended dietary allowances.*

	Thiamine	Riboflavin	Nicotinic acid	Ascorbic acid
Average for 110 foods*	5.0	5.4	41	2300
Recommended allowance†	1.30	1.83	17	66
Ratio	3.8	3.0	2.4	35

* From Table 1.

† Average for adults, male and female, referred to 2500 kcal food energy.[1]

per 2500 kcal of food energy) are nearly the same: 3.8, 3.0, and 2.4, respectively. It seems likely that the relative needs for these substances are nearly the same for plants as for animals. Also, they are apparently nearly the same for different kinds of plants. In Table 3 values are given relative to the amounts containing 41 mg of nicotinic acid. On this basis the amount of thiamine is close to 4.6 mg, except for beans and peas, and the amount of riboflavin is close to 5.5 mg, except for nuts and grains.

TABLE 3. *Water-soluble vitamin content (mg) of plant foods relative to nicotinic acid (41 mg).*

	Thiamine	Riboflavin	Ascorbic acid
Nuts and grains (11)	4.9	2.3	0
Beans and peas (15)	9.0	5.7	1200
Berries (8)	4.6	5.5	3300
Fruit (21)	4.1	4.3	1300
Vegetables (25)	5.3	6.2	1260
Intermediate-C foods (16)	4.2	5.2	1800
High-C foods (14)	4.6	6.6	6100

Ascorbic acid differs from the other vitamins in that most animal species continue to synthesize it despite its availability in natural foods. I think that the only reasonable explanation of this fact is that the foods available to most animals over the past several hundred million years have not provided a supply of ascorbic acid sufficient to justify the abandonment of the mechanism of its synthesis. We are accordingly able to make an estimate of the optimum daily intake of ascorbic acid, on the basis of this fact and the assumption that the foods listed in Table 1 represent approximately the foods available to the ancestors of existing animal species.

The average amount of ascorbic acid (per 2500 kcal energy value) for the 110 natural foods in Table 1 is 2300 mg. According to the foregoing argument, this amount is less than the optimum daily requirement of an adult animal requiring 2500 kcal of food energy.

I conclude that the optimum daily requirement of ascorbic acid for a human being requiring 2500 kcal of food energy is about 2.3 g (2300 mg) (2.6 g for an adult male, and 2.0 g for an adult female), or is greater than this amount.

We may ask how much greater the optimum daily requirement may be. The loss of the ability to synthesize ascorbic acid has occurred only four times in several hundred million years, so far as we know: in the common ancestor of man and other primates, about 25 million years ago; in the guinea pig; in one Indian fruit-eating bat; and in the ancestor of some Passeriform birds. The animals that underwent this change must have been living in an environment that provided an unusually great amount of ascorbic acid. I have listed in Table 1 fourteen natural foods that are unusually rich in this substance. They contain between 5.0 and 16.5 g of ascorbic acid for 2500 kcal energy value, with average 9.5 g. It is unlikely that the special environment mentioned above would provide only red sweet peppers (16.5 g), black currants (9.3 g), or broccoli spears (8.8 g); but the average of these fourteen foods, 9.5 g of ascorbic acid, might well have become available to a population of animals a few times during the period of several hundred million years preceding the present epoch. Accordingly, I conclude that it is unlikely that the optimum daily intake of ascorbic acid by human beings is greater than 9.5 g.

The range 2.3–9.5 g to which this evolution argument leads agrees moderately well with the values 2 g from Bourne's gorilla argument and 1.8–4.1 g from Stone's rat argument, and supports the suggestion by Bourne and the contention by Stone that the optimum rate of intake of ascorbic acid is many times the officially recommended daily dietary allowance, ranging in different countries from 20 to 75 mg. I have recently reached the conclusion that the state of health of most people, including the ability to resist infectious diseases such as the common cold, would be greatly improved by an increased intake of this important food.[15]

It is, of course, almost certain that some evolutionarily effective mutations have occurred in man and his immediate predecessors rather recently (within the last few million years) such as to permit life to continue on an intake of ascorbic acid less than that provided by high-ascorbic-acid raw plant foods. These mutations might involve an increased ability of the kidney tubules to pump ascorbic acid back into the blood from the glomerular filtrate (dilute urine, being concentrated on passage along the tubules) and an increased ability of certain cells to extract ascorbic acid from the blood plasma. It is likely that the adrenal glands act as a storehouse of ascorbic acid, extracting it from the blood when green plant foods are available, in the summer, and releasing it slowly when the supply is depleted. On general principles we can conclude, however, that these mechanisms require energy and are a burden to the organism. The average optimum rate of intake of ascorbic acid might still be close to the value given above, 2.3 g per day or more, or might be somewhat less; and, of course, there is always the factor of biochemical individuality, such that for different people in a large population the optimum intake might vary over a range of 20-fold or more.[16]

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